Gambel, Phillip

From: Gambel, Phillip
Sent: Friday, September 24, 2004 6:16 PM
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Subject: tnf and myelodysplastic syndrome 10 / 010,229

please provide the following references to

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thanx

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3/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007177089 BIOSIS NO.: 199089094980
MYELODYSPLASTIC SYNDROME MDS-ASSOCIATED INHIBITORY ACTIVITY ON HEMOPOIETIC PROGENITOR CELLS
AUTHOR: OHMORI M (Reprint); OHMORI S; UEDA Y; TOHYAMA K; YOSHIDA Y; UCHINO H
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JOURNAL: British Journal of Haematology 74 (2): p179-184 1990
ISSN: 0007-1048
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We studied MDS-associated inhibitory activity, which inhibited colony formation in vitro of granulocyte-macrophage progenitors (CFU-GM). Macrophages obtained from MDS bone marrow mononuclear cells (BM-MNC) when pretreated with granulocyte-macrophage colony stimulating factor (GM-CSF) suppressed the growth of normal CFU-GM. These macrophages were designated as 'MDS-derived inhibitory macrophages'. Media conditioned by MDS-derived inhibitory macrophages (MDS-CM) also suppressed the growth of normal CFU-GM. In the MDS-CM, high levels of prostaglandin E2 (PGE2) and ferritin were found. However, MDS-CM did not contain detectable levels of tumour necrosis factor (TNF) or gamma-interferon (.gamma.-IFN). Antiserum against human placentral ferritin and/or against PGE2 blocked the haemopoietic inhibitory activity to some extent. These results suggest that inhibitory macrophages may be responsible for the suppression of granulopoiesis in patients with MDS and that the suppression may be mediated by soluble factors including PGE2 and ferritin.

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3/7/9 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

05479988 EMBASE No: 1993248087
Induction of TNF-alpha in patients with myelodysplastic syndromes undergoing treatment with interleukin-3
Seipelt G.; Ganser A.; Duranceyk H.; Maurer A.; Ottmann O.G.; Hoelzer D.
Abteilung fur Hamatologie, Zentrum der Inneren Medizin, Klinikum Johann Wolfgang Goethe Univ, Theodor-Stern-Kai,6000 Frankfurt 70 Germany
British Journal of Haematology (BR. J. HAEMATOL.) (United Kingdom) 1993, 84/4 (749-751)
CODEN: BJHEA ISSN: 0007-1048
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The study was undertaken to analyse whether the presence or the induction of TNF-alpha, a potent inhibitor of haemopoiesis, might affect the clinical response to treatment with interleukin-3 in patients with myelodysplastic syndromes. A total of 15 patients were treated with IL-3. Baseline serum TNF-alpha levels were elevated in MDS patients (14.2 +/- 2.4 pg/ml) compared to healthy controls (9.1 +/- 1.1 pg/ml). During IL-3 therapy TNF-alpha levels remained unchanged in 3/14 patients in whom platelet counts increased, while in non-responders TNF-alpha levels increased 1.9-fold ($P < 0.025$). These findings indicate that TNF-alpha not only is induced during IL-3 therapy in MDS patients but that this elevation might be associated with a poor platelet response to therapy.

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3/7/12 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

05285939 EMBASE No: 1993054024
Measurement of serum cytokine levels in patients with myelodysplastic syndromes
Verhoef G.E.G.; De Schouwer P.; Ceuppens J.L.; Van Damme J.; Goossens W.; Boogaerts M.A.
Department of Hematology, University Hospital Gasthuisberg, Herestraat 49,3000 Leuven Belgium
Leukemia (LEUKEMIA) (United Kingdom) 1992, 6/12 (1268-1272)
CODEN: LEUKE ISSN: 0887-6924
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Sera of 25 healthy controls and 75 patients suffering from myelodysplastic syndromes (MDS) were investigated for serum concentration of interleukin-1alpha (IL-1alpha), IL-3, IL-6, granulocyte-colony-stimulating factor (G-CSF), granulocyte-macrophage-CSF (GM-CSF), erythropoietin (Epo), and tumor necrosis factor-a (TNFalpha). According to French-American-British (FAB) classification, 21 refractory anemia (RA), seven refractory anemia with ring sideroblasts (RARS), 15 chronic myelomonocytic leukemia (CMML), 12 refractory anemia with excess of blasts (RAEB), and 20 RAEB in transformation (RAEBt) were examined. TNF-alpha levels were inversely correlated with lower levels of hemoglobin concentration ($r=-0.31$, $p=0.005$), irrespective of the requirements for transfusion in anemic MDS patients. Significant differences in TNF-alpha levels between CMML (26.2+/-5.9pg/ml) and

the FAB subgroups (16.1+/-1.6pg/ml) were detected. There was an overall inverse relationship between the level of erythropoietin and the degree of anemia, but a wide range of Epo response between patients with similar hemoglobin concentrations. Serum levels of IL-1alpha and GM-CSF were undetected in most of the patients. In 57% of the samples there were detectable levels of G-CSF, without a correlation of the serum levels with blood cell counts, nor with any of the FAB subcategories. Overall, 29% and 25% of the patient sera exhibited elevated IL-3 and IL-6 levels, respectively. There was no correlation of the serum levels with any of the blood counts, other cytokines, nor FAB subcategories. In conclusion, simple negative feedback mechanism between a specific cytokine and the production of blood cells seems not to be the case in MDS, except for red cell production and erythropoietin concentration. Our data may suggest the involvement of TNF-alpha in the pathogenesis of anemia in MDS.

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5/7/2 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

06212421 EMBASE No: 1995241508
Modulation of acute graft-versus-host disease after allogeneic bone marrow transplantation by tumor necrosis factor A (TNFalpha) release in the course of pretransplant conditioning: Role of conditioning regimens and prophylactic application of a monoclonal antibody neutralizing human TNFalpha (MAK 195F)

Holler E.; Kolb H.J.; Mittermuller J.; Kaul M.; Ledderose G.; Duell T.; Seeber B.; Schleuning M.; Hintermeier-Knabe R.; Ertl B.; Kempeni J.; Wilmanns W.
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Blood (BLOOD) (United States) 1995, 86/3 (890-899)
CODEN: BLOOA ISSN: 0006-4971
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Contribution of host-related cytokine release in the course of pretransplant conditioning to early tissue damage and induction of acute graft-versus-host disease (GVHD) after allogeneic bone marrow transplantation (BMT) has been shown in experimental models. We performed a clinical phase I/II trial applying a monoclonal antibody neutralizing human tumor necrosis alpha (TNFalpha) during pretransplant conditioning as additional prophylaxis in high-risk patients admitted to allogeneic BMT; TNFalpha serum levels and clinical courses in 21 patients receiving anti-TNFalpha prophylaxis were compared with data from 22 historical controls. Absence of significant release of TNFalpha in the period of busulphan (BUS) treatment, but significant induction of TNFalpha by total body irradiation (TBI) and cyclophosphamide (CY) conditioning were correlated with significantly earlier onset of acute GVHD in patients receiving TBI/CY regimens as compared with BUS/CY-treated patients. Prophylactic application of monoclonal anti-TNFalpha seemed to postpone onset of acute GVHD from day 15 to day 25 ($P < .05$) after TBI/CY and from day 33 to day 53 after BUS/CY ($P < .10$) conditioning. Application of monoclonal anti-TNFalpha in low and intermediate doses was safe and not associated with an increased incidence of infectious or hematologic complications. Thus, our data provide indirect and direct evidence for involvement of conditioning-related cytokine release in induction of early acute GVHD in the clinical setting and support further investigation of this novel approach in randomized trials.

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5/7/1 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

11497294 EMBASE No: 2002068773
Infliximab chimaeric anti-tumour necrosis factor alpha monoclonal antibody treatment for patients with myelodysplastic syndromes
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British Journal of Haematology (BR. J. HAEMATOL.) (United Kingdom)
2002, 116/2 (334-337)
CODEN: BJHEA ISSN: 0007-1048
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 12

Tumour necrosis factor alpha (TNF-alpha) is believed to play a major role in apoptotic death of bone marrow cells in myelodysplastic syndromes (MDS). We explored the efficacy and safety profile of infliximab chimaeric anti-TNF-alpha monoclonal antibody treatment in two MDS patients. They both had low-/intermediate-risk MDS, isolated anaemia and elevated circulating levels of TNF-alpha. Infliximab produced no adverse side-effects and resulted in sustained erythroid responses, one major and one minor. Laboratory studies indicated a remarkable decrease in the percentage of apoptotic stem cells in the bone marrow. This preliminary report indicates that infliximab may have an application as MDS therapy and warrants further investigation.